

Applicants: Michael R. Rosen, et al
U.S. Serial No. 09/898,417
Filed: July 3, 2001
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c) Listing of Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently Amended) A method of assaying whether an agent affects heart rate of a cardiac cell which comprises:
- (a) contacting a cardiac cell ~~of a heart~~ with an effective amount of a compound in vitro to cause a sustainable heart rate;
 - (b) measuring the heart rate after step (a);
 - (c) contacting ~~providing~~ the cardiac cell ~~heart~~ with an agent to be assayed for its effects ~~affects~~ on heart rate;
 - (d) measuring the heart rate after step (c); and
 - (e) comparing the difference between step (b) and step (d), thereby determining whether the agent affects heart rate.
2. (Original) The method of claim 1, wherein the heart is mammalian.
3. (Original) The method of claim 1, wherein the cardiac cell is a cardiac myocyte.
4. (Withdrawn)
5. (Withdrawn)
6. (Withdrawn)
7. (Withdrawn)
8. (Withdrawn)
9. (Currently Amended) The method of claim 1, wherein the compound comprises nucleic acids which encodes MiRP1 and a HCN channel.
10. (Withdrawn)

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11. (Original) The method of claim 9, wherein the HCN is HCN2.
12. (Withdrawn)
13. (Canceled)
14. (Canceled)
15. (Currently Amended) A method of assaying whether an agent affects heart rate which comprises:
- (a) disaggregating in vitro cardiac myocytes ~~myocytes~~ from a heart;
 - (b) measuring the beating rate of the cardiac myocytes after step (a);
 - (c) contacting a set of the cardiac myocytes from ~~form~~ step (a) with an agent to be assayed for its effects on heart rate;
 - (d) measuring the heart rate after step (c); and
 - (e) comparing the measurements from step (b) and step (d), thereby determining whether the agent affects heart rate.
16. (Original) The method of claim 15, wherein the measuring steps are performed with a calcium sensitive dye and a photodiode.
17. (Withdrawn)
18. (Withdrawn)
19. (Withdrawn)
20. (Withdrawn)
21. (Withdrawn)
22. (Withdrawn)
23. (Withdrawn)
24. (Withdrawn)

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25. (Withdrawn)

26. (Withdrawn)

27. (Withdrawn)

28. (Withdrawn)

29. (Withdrawn)

30. (Withdrawn)

31. (Withdrawn)

32. (New) The method of claim 1, wherein the contacting is performed by administration of an adenovirus infection, viral-mediated infection, liposome-mediated transfer, microinjection, electroporation, or coculturing the cell with a nucleic acid encoding MiRP1 and HCN.

33. (New) The method of claim 32, wherein the HCN is HCN1.

34. (New) The method of claim 32, wherein the HCN is HCN2.

35. (New) The method of claim 32, wherein the HCN is HCN4.

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d) Amendments to the Abstract:

Please replace the current abstract, beginning on page 78, line 4, with the following new abstract:

AP
This invention provides for a chamber and system designed for use in assaying drug effects on heart rate. The chamber consists of a series of wells, ~~each 3mm by 3mm in inner diameter~~. Cardiac myocytes disaggregated from neonatal animals are plated onto the bottom of each well and grown under standard tissue culture conditions. ~~The chamber holds from 24-96 such wells~~. When drugs are to be assayed, the cells in each well are loaded with a calcium sensitive dye and the beating rate in each is monitored with a photodiode. A ~~D~~drug is added in graded concentrations to each well, and equilibrated and effects on rate are observed. This construct permits use of a cell based bioassay for the study of drugs or agents that may alter cardiac rate. This invention can be used in high throughput screening of drugs to evaluate/predict their effects on cardiac rate and rhythm. ~~Further provided for by this invention is a A vector which comprises a compound which encode an ion channel.~~

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e) Amendments to the Drawings:

Please replace original drawings (Sheets 1-17) with new drawings
(Sheets 1-29) attached hereto as **Exhibit A**.